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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,191	09/23/2005	Shinji Iijima	12218/46	6125

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KENYON & KENYON LLP
1500 K STREET N.W.
SUITE 700
WASHINGTON, DC 20005

EXAMINER	
HILL, KEVIN KAI	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/523,191	**Applicant(s)** IIJIMA ET AL.	
	Examiner KEVIN K. HILL	**Art Unit** 1633	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 17 June 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *6* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-6,9-31,33-40 and 42-56*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: See Continuation Sheet.

/Q. JANICE LI, M.D./
Primary Examiner, Art Unit 1633

Continuation of 13. Other: Continuation of 11. does NOT place the application in condition for allowance because: Claims 1-6, 8-31 and 33-56 stand rejected for reasons of record in the Office Action mailed March 17, 2008. Applicant requests reconsideration after Final Office Action. The request for reconsideration has been entered but is moot because the amendment does not overcome that cited prior art.

Response to Arguments
With respect to the rejection of claims 1 and 25 under 35 U.S.C. 112, second paragraph, Applicant argues that the disclosure is sufficiently definite to make clear the "metes and bounds" of the term "derived from.", e.g. "5'LTR and 3'LTR each represents a long terminal repeat sequence of MoMLV".
Applicant's argument(s) has been fully considered, but is not persuasive. Those of ordinary skill in the art recognize that the MoMLV genome is composed of, and identified by, nucleic acid sequences in addition to the 5' and 3' LTRs. The instant claims do not require the MoMLV 5'LTR and 3'LTR. Rather, the breadth of the claim reasonably embraces any nucleic acid sequence obtained from a wildtype MoMLV genome, as well as any derivation thereof, e.g. an unspecified number of substitutions, insertions or deletions, to the extent that one of ordinary skill in the art would not immediately recognize the final product nucleic acid sequence as necessarily being "derived from" a wildtype MoMLV genome.

With respect to the rejections under 35 U.S.C. 102, Applicant argues that:
a) neither Ivarie et al nor Rapp et al actually disclose the production of transgenic birds with exogenous antibody genes.
b) an essential feature of the invention is that virus infection is carried out after and exclusive of a blastodermal period, which enables one to achieve sufficient expression of exogenous transgene. This feature is not disclosed in any of the references. The transgene expression in the present application is more efficient than that in the references. The amount of transgene expression in eggs is not disclosed in the references. The fact that the amount of transgene expression in the eggs of GO birds is far more than the amount disclosed in the references is at least some evidence that the transgenic birds in the product-by-process claims 1-23, and its dependent claim 24, are structurally distinct from those in the cited references.
Applicant's argument(s) has been fully considered, but is not persuasive.
With respect to a), "When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. In re Sasse, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). See also MPEP §716.07." In the instant case, Applicant has provided no evidence that that the cited prior art is inoperable.
With respect to b), "A prior art reference provides an enabling disclosure and thus anticipates a claimed invention if the reference describes the claimed invention in sufficient detail to enable a person of ordinary skill in the art to carry out the claimed invention; "proof of efficacy is not required for a prior art reference to be enabling for purposes of anticipation." Impax Labs. Inc. v. Aventis Pharm.Inc., 468 F.3d 1366, 1383, 81 USPQ2d 1001, 1013 (Fed. Cir. 2006). See also MPEP §2122.<" In the instant case, the cited prior art disclose antibody concentration ranges that embrace the instantly recited antibody concentration ranges in the instantly recited tissues, and thus the efficacy of transgene expression is considered indistinguishable from the instantly claimed invention given that the yield of the desired antibody product from the transgene is also indistinguishable from the instantly claimed invention.

With respect to the rejections under 35 U.S.C. 103, Applicant argues that:
a) the transgenes used by Ivarie et al and Rapp et al (β-lactamase and interferon) are different from the transgene in the present invention (antibody). It is well known to one skilled in the art that the amount of gene expression varies according to the gene used. It is incorrect to conclude that that the degree or mechanism of transgene silencing is not germane by simply comparing the amount of transgene expression in the references that use different transgenes from the instant application with the amount of transgene expression in the instant application.
b) Mizuarai does not recognize or suggest the unexpected effect of enhancing transgene expression imparted by infecting an early embryo. Without a recognition of this unexpected effect, there is no reason to modify any of the above references to infect the embryo after and exclusive of a blastodermal period immediately after the spawning with a replication-defective retrovirus vector.
Applicant's argument(s) has been fully considered, but is not persuasive.
With respect to a), the instant claims embrace an enormous genus of structurally distinct antibody genes encoding structurally distinct antibody molecules. Applicant has provided no evidence that full-length antibodies are expressed from a transgene with equal and predictable efficacy as scFv antibody fragments, for example. Furthermore, the cited prior art teaches transgenes encoding antibodies. Thus, the antibody transgenes of the prior art must necessarily achieve the amount of gene expression as the instantly recited antibody transgenes because they are "antibody genes" as argued by Applicant, and are structurally indistinguishable from the instantly claimed antibody genes.
With respect to b), In response to applicant's argument that an unexpected effect of enhancing transgene expression is imparted by infecting an early embryo exclusive of a blastodermal period, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See Ex parte Obiaya, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). In the instant case, those of ordinary skill in the art need not have the same reasons as Applicant to produce transgenic birds as per the instantly recited method steps. As discussed in the corresponding rejection, an artisan would be motivated to infecting an early embryo exclusive of a blastodermal period because Mizuarai et al teach the addition of protamine-modified lipid vesicles to pantropic retroviral particles increased the viral titer 12-fold, and that the cationic lipid can effectively mediate the virus-cell interaction in the presence of serum and enhance retroviral transduction (pg 130, col.s 1-2). Mizuarai et al suggest that in vivo gene transfer using protamine-modified lipid vesicles may be established as a safe and efficient method for gene delivery (pg 131, col. 1, last sentence). Enhanced transgene expression would naturally flow from the process of making

transgenic birds because it is a biological phenomena, inseparable from the organism, in response to infecting an early embryo exclusive of a blastodermal period as taught by Mizuarai et al.

With respect to the provisional nonstatutory obviousness-type double patenting rejections, Applicants have indicated that they will deal with these rejections after the present claimed are deemed otherwise allowable. However, it is noted that the provisional obviousness-type double patenting rejection will be maintained until the aforementioned issues are resolved. .